Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for selecting a combination of therapeutic agents for treatment of a disease caused by an abnormal cell signaling pathway or cell signaling pathway network that leads to an aberrant cellular response, comprising:

measuring activity states for a plurality of different signaling proteins extracted from a diseased cell, wherein the signaling proteins are members of one or more signaling pathways or networks;

measuring activity states for a plurality of different signaling proteins extracted from a reference cell, wherein the signaling proteins are members of one or more signaling pathways or networks;

determining whether the activity states measured for the plurality of signaling proteins extracted from the diseased cell are different than activity states measured for corresponding signaling proteins from the reference cell to detect differences between the activity states of individual signaling proteins from the diseased cell and the activity states of the corresponding individual signaling proteins from the reference cell; and

selecting a combination of at least two different therapeutic agents, ~~wherein the selected therapeutic agents target two or more different members of a protein signaling pathway or network comprising an individual signaling protein for which a difference in activity state was detected between the diseased cell and the reference cell,~~ wherein the agents reduce the difference **that was detected** in the activity state**s of the individual signaling proteins from the diseased cell compared to the reference cell** ~~that was detected~~.

2. (Currently Amended) The method of claim 1, wherein the combination of therapeutic agents provides a synergistic improvement in efficacy of treatment of the aberrant cellular response when compared **to** the combined efficacies of the agents administered alone at the same dose.

3. (Original) The method of claim 1, wherein the diseased cell is obtained from tissue of a subject, the method further comprising isolating the diseased cell from the tissue of the subject.

4. (Original) The method of claim 3, wherein isolating the diseased cell comprises microdissection of the diseased cell from the tissue.

5. (Original) The method of claim 4, wherein microdissection comprises laser capture microdissection.

6. (Withdrawn) The method of claim 3, wherein isolating the diseased cell comprises isolating the diseased cell by fluorescence activated cell sorting.

7. (Original) The method of claim 1, further comprising extracting the plurality of different signaling proteins from a cell sample comprising the diseased cell.

8. (Withdrawn) The method of claim 7, wherein the cell sample is a sample of cells obtained by microdissection.

9. (Previously Presented) The method of claim 7, wherein the cell sample is a sample of cells obtained by laser capture microdissection.

10. (Withdrawn) The method of claim 1, wherein measuring the activity states of the plurality of signaling proteins comprises measuring the activity states using protein microarray analysis, immunohistochemistry, antibody microarray analysis, or bead capture.

11. (Currently Amended) The method of claim 1, wherein measuring the activity states of the plurality of signaling proteins **extracted from the diseased cell and the reference cell** comprises using reverse phase protein microarray analysis.

12. (Original) The method of claim 11, wherein the reverse phase protein microarray analysis comprises microarray analysis of phosphorylated signaling proteins using antibodies that specifically bind to a particular phosphorylated signaling protein.

13. (Withdrawn) The method of claim 12, wherein the microarray analysis comprises microarray analysis of total amounts of signaling proteins using antibodies that specifically bind to particular signaling proteins regardless of their phosphorylation state, and the activity state of the signaling protein is determined as a ratio of the phosphorylated signaling protein to the total amount of the signaling protein.

14. (Original) The method of claim 1, wherein the reference cell is a normal cell, a cell before or after a treatment, or a cell before or after a disease or a stage of disease.

15. (Original) The method of claim 14, wherein the reference cell is a normal cell.

16. (Withdrawn) The method of claim 14, wherein the reference cell comprises a cell that has not been treated with a therapeutic agent.

17. (Original) The method of claim 1, wherein the diseased cell and the reference cell are obtained from the same subject.

18. (Withdrawn) The method of claim 1, wherein the reference cell is obtained from one subject and the diseased cell is obtained from another subject.

19. (Withdrawn) The method of claim 1, wherein one or both of the reference cell and the diseased cell are cultured cells.

20. (Original) The method of claim 1, further comprising administering the combination to a subject from which the diseased cell was obtained.

21. (Currently Amended) The method of claim 1, wherein the aberrant cellular response comprises abnormal growth, apoptosis, cytoskeletal remodeling, survival, receptor

localization and distribution, gene transcription, motility, differentiation, proliferation, **inflammation** or angiogenesis.

22. (Original) The method of claim 1, wherein the measured activity states of the signaling protein comprises one or more of a protein-protein interaction, a post-translational modification, a protein cleavage, a translocation to an organelle or compartment, an ion channel activation, a concentration of a soluble mediator that is a product or a substrate of the protein, a protein-nucleic acid interaction, a protein-lipid interaction, or a protein-carbohydrate interaction.

23. (Previously Presented) The method of claim 22, wherein the post-translational modification comprises phosphorylation, farnesylation, myristylation, acetylation or ubiquitinization.

24. (Previously Presented) The method of claim 1, wherein the combination is selected based on prior success in reducing the difference in the detected activity state in a subject having a same difference in activity state for one or more individual signaling proteins as is determined in a subject from which the diseased cell was obtained.

25. (Original) The method of claim 1, wherein determining differences between the activity states of the plurality of signaling proteins between the diseased cell and the reference cell comprises pattern recognition.

26. (Original) The method of claim 1, wherein the combination of therapeutic agents comprises two or more of drugs that separately target a combination of EGFr dimerization, EGFr phosphorylation, AKT phosphorylation, non-voltage gated calcium ion channels, cyclooxygenase- 1, cyclooxygenase-2, MEK-1, NFKB/IKB, and P38.

27. (Original) The method of claim 1, wherein the combination prevents shunting to or around a signaling pathway.

28. (Withdrawn) The method of claim 27, wherein the combination includes a drug that inhibits MEK phosphorylation of ERK kinase, and shunting occurs via activation and phosphorylation of CREB.

29. (Original) The method of claim 1, wherein the combination comprises a prostaglandin pathway effector and a non-voltage gated calcium influx channel effector.

30. (Original) The method of claim 1, wherein the combination comprises CaI and a specific COX-2 inhibitor.

31. (Original) The method of claim 30, wherein the specific COX-2 inhibitor comprises Rofecoxib, Celecoxib or LM- 1685.

32. (Withdrawn) The method of claim 1, wherein the combination comprises an AKT kinase inhibitor and either an EGFR dimerization inhibitor or an EGF kinase inhibitor.

33. (Withdrawn) The method of claim 32, wherein the EGF dirnerization inhibitor comprises herceptin and the EGF kinase inhibitor comprises IRESSA.

34. (Withdrawn) The method of claim 1, wherein the combination comprises a PKCalpha agonist resulting in phosphorylation and activation of PKCalpha.

35. (Withdrawn) The method of claim 32, wherein the combination comprises an AKT kinase inhibitor and herceptin.

36. (Original) The method of claim 1, wherein the disease comprises a neurodegenerative disease, memory loss or cancer.

37. (Currently Amended) The method of claim 36, wherein the disease ~~comprises~~ **is selected from the group consisting of:** breast cancer**, lung cancer, and** ~~or~~ colon cancer.

38. (Original) The method of claim 1, wherein one or more of the signaling proteins in the plurality of different signaling proteins are members of an integrin pathway, a focal

adhesion signaling pathway, an Akt signaling pathway, an IL-6R pathway, a growth factor pathway, a chemokine receptor signal pathway, a cell-cycle signaling pathway, a stress signal pathway, an apotosis signaling pathway, a Taubet a signaling pathway, a pro-inflammatory pathway, a differentiation signaling pathway, a T-cell receptor pathway, a death-receptor signaling pathway, a survival signaling pathway, a MAPK signaling pathway, a p38 MAPK signaling pathway, a G coupled Receptor signaling pathway, a SAPKIN signaling pathway, an insulin receptor signaling pathway, a Wnt signaling pathway, a c-Kit pathway, a c-kit signaling pathway, a B-cell antigen signaling pathway, or a JaMStat signaling pathway.

39. (Currently Amended) The method of claim 1, wherein the activity state is phosphorylation of the signaling protein and measuring comprises determining a ratio of the amount of phosphorylated signaling protein to **either the total amount of protein or** the total amount of signaling protein.

40. (Previously Presented) The method of claim 1 further comprising repeating the steps of claim 1 for a second diseased cell obtained from a subject or a cell culture during or following administration of the combination to the subject or the cell culture and combining at least one additional therapeutic agent with the combination to make a second combination, wherein the at least one additional therapeutic agent in the second combination reduces a difference in the activity state that was detected by repeating the steps of claim 1.

41. (Original) The method of claim 1, wherein the difference in activity states detected is an increase in the activity state of an individual signaling protein from the diseased cell in comparison to the same signaling protein in the reference cell, and the therapeutic agents are selected to counteract the increase in the activity state of the individual signaling protein from the diseased cell.

42. (Original) The method of claim 41, wherein the increase in activity state of the individual signaling protein from the diseased cell is an increase in phosphorylation and the

therapeutic agents are selected to counteract the increase in phosphorylation of the individual signaling protein from the diseased cell.

43. (Original) The method of claim 1, wherein the difference in activity states detected is a decrease in the activity state of an individual signaling protein from the diseased cell in comparison to the same signaling protein in the reference cell, and the therapeutic agents are selected to counteract the decrease in the activity state of the individual signaling protein from the diseased cell.

44. (Original) The method of claim 43, wherein the decrease in activity state of the individual signaling protein from the diseased cell is a decrease in phosphorylation and the therapeutic agents are selected to counteract the decrease in phosphorylation of the individual signaling protein from the diseased cell.

45-50. (Canceled)

51. (Currently Amended) A method for selecting a combination of therapeutic agents for treatment of a disease caused by a abnormal cell signaling pathway or a cell signaling pathway network that leads to an aberrant cellular response, comprising:

measuring activity states for a plurality of different signaling proteins extracted from a diseased cell obtained from a subject, wherein the signaling proteins are members of one or more signaling pathways or networks;

determining whether the activity states measured for the plurality of signaling proteins extracted from the diseased cell are different than activity states measured for corresponding signaling proteins from a reference cell to detect differences between the activity states of individual signaling proteins from the diseased cell and the activity states of the corresponding individual signaling proteins from the reference cell, wherein measuring the activity states of the plurality of signaling proteins comprises using reverse phase protein microarray analysis of phosphorylated signaling proteins using antibodies that specifically bind to a particular phosphorylated signaling protein; and

selecting a combination of at least two different therapeutic agents ~~that target two or more different members of a protein signaling pathway or network comprising an individual signaling protein for which a difference in activity state was detected between the diseased cell and the reference cell~~, wherein the agents reduce the difference **that was detected** in the activity state**s of the individual signaling proteins from the diseased cell compared to the reference cell** ~~that was detected~~**, and wherein the combination of therapeutic agents provides a synergistic improvement in efficacy of treatment of the aberrant cellular response when compared to the combined efficacies of the agents administered alone at the same dose**.

52. (Previously Presented) The method of claim 51, wherein the diseased cell is obtained from tissue of the subject, the method further comprising isolating the diseased cell from the tissue of the subject.

53. (Previously Presented) The method of claim 52, wherein isolating the diseased cell comprises microdissection of the diseased cell from the tissue.

54. (Previously Presented) The method of claim 53, wherein microdissection comprises laser capture microdissection.

55. (Previously Presented) The method of claim 51, further comprising measuring activity states for a plurality of different signaling proteins extracted from the reference cell, wherein the signaling proteins are members of one or more signaling pathways or networks.

56. (New) A method for selecting a combination of therapeutic agents for treatment of a disease caused by an abnormal cell signaling pathway or cell signaling pathway network that leads to an aberrant cellular response, comprising:

measuring post-translational modifications of a plurality of different signaling proteins extracted from a diseased cell, wherein the signaling proteins are members of one or more signaling pathways or networks;

measuring post-translational modifications of a plurality of different signaling proteins extracted from a reference cell, wherein the signaling proteins are members of one or more signaling pathways or networks;

detecting differences between the post-translational modifications of individual signaling proteins from the diseased cell and the post-translational modifications of the corresponding individual signaling proteins from the reference cell; and

selecting a combination of at least two different therapeutic agents, wherein the agents reduce the difference that was detected in the post-translational modifications of the individual signaling proteins from the diseased cell compared to the reference cell, and wherein the combination of therapeutic agents provides a synergistic improvement in efficacy of treatment of the aberrant cellular response when compared to the combined efficacies of the agents administered alone at the same dose.

57. (New) The method of claim 56, wherein the measuring post-translational modifications of a plurality of different signaling proteins extracted from the diseased or reference cell comprises measuring the phosphorylation state of the plurality of signaling proteins.

58. (New) The method of claim 56, wherein measuring the post-translational modifications of the plurality of signaling proteins extracted from the diseased cell and the reference cell comprises using reverse phase protein microarray analysis.